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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/843,126	04/26/2001	Peter C. Astles	CA2413US NP	8340

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/843,126	ASTLES ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *14 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment and response filed by applicants in paper No. 9, dated Oct. 14, 2003 have been entered and considered carefully.

2. Applicants allegation that the examiner improperly made the present restriction requirement final because the examine should allow applicants with an opportunity to respond again.

It is noted that in Paper No. 2, office action with respect to restriction it was clearly advised that (p.3):

> "Groups I and II are distinct because the compounds of group I and group II differ in elements, bonding arrangements and chemical properties to such an extend that a reference anticipating compounds of group I would not necessarily render compounds of group II obvious. The search for compounds of group I is not required for group II and vice versa. The method of treatment of group II is independent and distinct because method of treating the independent and distinct disease for example asthma and ulcer are disease and symptom oriented. Each method must be searched/examined on its merit. The composition and method of treatment using multiple active ingredients of group IV are independent since the combination can be synergistic, parallel or in independent functionality (see CA 110. CA 132). The basis for merit examination and searches for such distinct combination are not coextensive thus separate examinations must be conducted.
>
> Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).
>
> Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention. In the instant case, then there could have been no patentability of all the claims over Pieper et al. CA 122.

Please note that the reasoning and legal foundation for restriction were ***explicitly articulated*** based on ***factual evidence*** (see CA 110, 132, 122 supplied to applicants).

It is noted that in Paper No. 8, office action, in *answering to* applicant's traversal, it was clearly explained (p.2-3):

Applicant's election with traverse of group I, (claim 50, p.158, line 21, elected species in group I) in Paper No. 7, dated mar. 17, 2003 is acknowledged. The traversal is on the ground that the claims are drawn to Markush format thus variable ring size is not repugnant to principles of scientific classification. This is not found persuasive because applicants presented mere argument *without* factual evidence that the instant variable ring compounds share a substantial structural feature disclosed as being essential to the claimed utility.

Applicants attention is drawn to MPEP 803.02 restriction of Markush claims:" Broadly, unity of invention exists where compounds included within a Markush group (1)share a common utility ***and*** (2) share a substantial structural feature disclosed as being essential to that utility". The restriction was made based on that each different core structure have diverse utility for example, the pyrrolidinyl ring compounds are intermediates for making antibacterial (see US 5,342,844 col.16 example J), the seven membered ring compounds are antimicrobial (see CA128). Applicants presented mere arguments ***without*** factual evidence that diverse ring members responsible for diverse utility are obvious variants for the tryptase inhibition. Further, the specification on pages 147-148 disclosure support that this exclusive tryptase inhibitory activity is limited only to the piperidinyl compounds.

With respect to group IV, composition of multiple active ingredients are patentably distinct and unrelated to the other groups has been clearly delineated with factual evidence in the previous office action (see p.3 office action and citation of PTO-892). It was clearly evidenced by CA 132 that the combination of tryptase inhibitor and steroids would lead to synergistic decrease of mast cell activation while combination of tryptase inhibitor with adrenergic compounds (CA 110) would be counteracting on the smooth muscle relaxation. Therefore, not only combination of active ingredients is not obvious variants of single active ingredient composition but also such combination ***do not share any commonality*** of utility without specifically naming the class of active ingredients to be combined.

Applicants were advised that "Should applicant traverse on the ground that the groups and species are not patentably distinct, applicant should submit *evidence* or identify such evidence now of record showing the groups and species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention." For which applicants provided neither evidence nor admission. Were admission of such obvious variation, then there could have been no patentability of all the claims over US 5,342,844 col.16 example J because example J is an N- benzyl protected compound of the claims while the claims are drawn to the alternative conventional N-benzoyl protected compounds. A clear establishment of prima facie obviousness over the variation of N-protecting compounds.

The requirement is still deemed proper and is therefore made FINAL.

Therefore, applicants have offered clear legal foundation and detailed articulation of the reasoning together with ***factual evidence*** in the above record and applicants were clearly advised to substantiate any traversal with ***factual evidence*** or ***admission***. Failure in traversal on a timely manner when factual evidence have been provided and explained to applicants, can not be justified on given continuous opportunity to respond. The finality of the restriction was proper.

Claims 1-35, 51, 53-54 when n=0, 1, 3 or 4 and claims 64-72 being drawn to the non-elected invention, stayed withdrawn from consideration, and should be canceled.

3. The rejection under 35 USC 112 second paragraph with respect to the term "comprising" is dropped in view of the amendment.

The rejection of claims 51-52 under 35 Usc 112 second paragraph with respect to the quantitative definition is maintained for the following reason. Applicants have inserted the term "pharmaceutically acceptable amount". What does it mean? What is considered as pharmaceutically acceptable amount? No antecedent basis or descriptive support can be found in the specification. A new matter rejection will also be necessitated.

The rejection of claims 53-55 under 35 Usc 112 second paragraph with respect to the quantitative definition is maintained for the following reason. Applicants have inserted the term "pharmaceutically acceptable amount". What does it mean? What is considered as pharmaceutically acceptable amount? No antecedent basis or descriptive support can be found in the specification. A new matter rejection will also be necessitated.

4. Claims 51-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The term "pharmaceutically acceptable amount" lacks antecedent basis and descriptive support from the specification, thus, is NEW MATTER.

Removal of all new matter is required. In re Ressmussen 211 USPQ 325.

5. The rejection of claims 1-5, 709, 11-19, 21-23, 26-27, 30-34, 36-38, 40-41, 44-48 under 35 USC 103(a) over Pieper US 5,442,064 is maintained for reason of record.

Applicants argued that the Pieper '064 reference is limited to N-linkage therefore motivation for modification is lacking. Please note that the portion of Pieper '064 recited by applicants also taught that the 4-position of the cylcohexyl/cyclohexenyl ring can be N and with many examples as pointed out in the previous office action with explicit structural delineation of final products and starting material together with CA registry numbers. Applicants offered no explanation that why the broad genus which encompassed the more limited scope of the instant claims would be not in possession of artisan in the field or expected to have Pieper '064 activity as disclosed.

6. The rejections of claims 1-63 under the judicially created doctrine of obviousness type double patenting over US2002/0045613 in view of US 5,639,321 or 2002/0055522 is maintained for reason of record. No acceptable terminal disclaimer has been filed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane, can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Mar. 15, 2004

Celia Chang
Primary Examiner
Art Unit 1625